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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/634,732 | 08/03/00 | UMANSKY S | 20811-000111 |

HM12/0717
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| EXAMINER | |
|---|---|
| LU, F | |
| ART UNIT | PAPER NUMBER |
| 1655 | 6 |

DATE MAILED: 07/17/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/634,732 | Applicant(s) UMANSKY ET AL. | |
|---|---|---|---|
| | Examiner Frank W Lu | Art Unit 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-14,27,28 and 30-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-26 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/230,704* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Location of Application*

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1655.

### *Election/Restriction*

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CAR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I , claims 1-14, 27, 28, and 30-44, drawn to a method of detecting cancer in a patient (claims 1-14), a method of monitoring cancer treatment in a patient (claim 27), a diagnostic kit for detecting a genetic mutation indicative of cancer in the DNA of a patient (claim 28), and a method of analyzing a target nucleic acid sequence in urine (claims 30-44).

Group II , claims 15-26 and 29, drawn to a method of monitoring transplanted material in a patient (claims 15-26) and a diagnostic kit for detecting DNA from a transplanted material in the urine of a patient (claim 29).

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I and II do not relate to a single general inventive concept because they lack the same or corresponding special technical features. For example, group I does not need to search nucleic acid from transplanted material in a urine sample while group II does not need to search nucleic acid indicative of cancer in a urine sample.

During a telephone conversation with Mr. M. Henry Heines (Reg. No. 28,219) on July 5, 2001 a provisional election was made with traverse to prosecute the invention of Group II, claims 15-26 and 29. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-14, 27, 28, and 30-44 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Priority***

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37

CFR 1.78). For example, 60/048,170, 60/048.381, and PCT/US/10965. Applicant also need to update the status of 09/230,704.

***Drawings***

4. The drawings are objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

***Sequence Rules Compliance***

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Direct the reply to the undersigned.

***Claim Rejections - 35 U.S.C. § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 15-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claim 16-26 are dependent on claim 15.

Claim 15 is rejected as vague and indefinite what it intended. Note that not all cells from transplanted material that are found in urine need to cross the kidney barrier. For example, the cells from transplanted kidney can be found in urine.

***Claim Rejections - 35 U.S.C. § 102/103***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 15-19, 21, and 22 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lisby *et al.*, (APMIS, 102, 690-694, 1994).

Lisby *et al.*, teach PCR as a rapid diagnostic assay for HCMV infection in renal transplant patients. In this study, DNA in an urine sample was isolated and used to amplify the immediate early antigen of HCMV (see abstract in page 690, page 691 and Figure 1 in page 692). Note that: (1) amplified immediate early antigen of HCMV could be considered as a nucleic acid sequence that had crossed the kidney barrier and that was not present in the patient prior to transplantation as described in claim 15 since "infection due to cytomegalovirus is an important and frequent complication after renal transplantation" (see page 690, left column); and (2) boiling step in DNA isolation (see page 691, left column) could be considered to reduce DNA degradation as described in claim 19.

Therefore, Lisby *et al.*, teach the limitations recited by claims 15-19 and 22.

Alternatively, although Lisby *et al.*, did not show to use an urine sample that had been held in the bladder less than 12 hours as described in claim 21, in the absence of an unexpected result, one having ordinary skill in the art at the time the invention could optimize experimental conditions to reach these goals.

11. Claims 19-23 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Schatzl *et al.*, (J. Med. Virology, 42, 138-145, 1994).

Schatzl *et al.*, teach the detection of human polyomaviruses BK (BKV) and JC (JCV) in urine of three recipients with bone marrow transplantation. In this study, DNA in an urea sample was isolated by ethanol precipitation and used to amplify BKV and JCV DNA sequences (see pages 139 and 142). Note that: (1) amplified BKV or JCV DNA sequence could be considered as a nucleic acid sequence that had crossed the kidney barrier and that was not present in the patient prior to transplantation as described in claim 15 since BKV and JCV could not be detected before the transplantation; and (2) proteinase K or/and SDS used in DNA isolation (see page 691, left column) could be considered to reduce DNA degradation as described in claim 19 or/and 20.

Therefore, Schatzl *et al.*, teach the limitations recited by claims 15-20, 22, and 23.

Alternatively, although Schatzl *et al.*, did not show to use urine sample that had been held in the bladder less than 12 hours as described in claim 21, in the absence of an unexpected result, one having ordinary skill in the art at the time the invention could optimize experimental conditions to reach these goals.

12. Claims 25 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzl *et al.*, (1994) as applied to claims 15-20, 22, and 23 above, and further in view of Sorenson *et al.*, (US Patent No. 6,020,124, filed on June 7, 1995).

The teachings of Schatzl *et al.*, have been summarized previously, *supra.*

Schatzl *et al.*, do not disclose to filter an urine sample as described in claim 25 and a diagnostic kit for detecting DNA from a transplanted material in the urine as described in claim 29.

Sorenson does teach to filter an urine sample (elutip in column 14, second and third paragraphs) and a diagnostic kit for detecting DNA in the urine from a cancer patient. Such kits included reagents for the isolation of DNA as well as sets of primers used in the detection method, and reagents useful in the amplification including a DNA polymerase used to effect the amplification. Preferred polymerases were *Thermus aquaticus* DNA polymerase available from Perkin-Elmer as AmpliTaq DNA polymerase and AmpliTaq Stoffel fragment DNA polymerase (column 11, fourth paragraph and claims 22 and 23 in this prior art as shown in columns 29 and 30).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have filtered an urine sample from transplanted patient and organized the components and method taught by Schatzl *et al.*, and Sorenson into a kit because: (1) filtering the urine sample could provide a conventional way to remove contaminants; and (2) the kit format was utilized not only assemble a variety of different reagents together but ensured the quality and compatibility of the reagents. Sorenson would have motivated and suggested the assemblage of reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages, thus resulting in instant kit described in claim 29. One having ordinary skill in the art at the time the invention was made would have been

a reasonable expectation of success to combine these prior art together because all of these prior art are known and are easy to use.

13. Claims 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzl *et al.*, (1994) as applied to claims 15-20, 22, and 23 above, and further in view of Padhye *et al.*, (US Patent No. 5,808,041, filed on June 7, 1995).

The teachings of Schatzl *et al.*, have been summarized previously, *supra.*

Schatzl *et al.*, do not disclose to isolate nucleic acid by absorption on a resin as described in claim 24.

Padhye *et al.*, do teach to isolate nucleic acid by absorption on a resin (see column 11-14).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have isolated nucleic acid in an urine sample from transplanted patient by absorption on a resin as suggested by Padhye *et al.*. One having ordinary skill in the art would have motivated to modify the methods of Schatzl *et al.*, because the simple replacement of one well know nucleic acid isolation method (using precipitation) from another well know nucleic acid isolation method (using a column with a resin) would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

14. Claims 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzl *et al.*, (1994) and Sorenson (1995) as applied to claims 15-23, 25, and 29 above, and further in view of Bogdahn *et al.*, (US Patent No.5,770,366, filed on January 19, 1996).

The teachings of Schatzl *et al.*, and Sorenson have been summarized previously, *supra.*

Schatzl *et al.*, do not disclose to filter DNA large than 1000 bp.

Bogdahn *et al.*, teach to filter virus supernatant to remove any molecule large than 100 bp (Microcon 100, see column 19).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have filtered nucleic acid large than 1000 bp in an urine sample from transplanted patient as suggested by Bogdahn *et al.*. One having ordinary skill in the art would have motivated to modify the methods of Schatzl *et al.*, because the simple replacement of one filtration system (elutip) from another filtration system (Microcon 100) in order to remove DNA large than 1000 bp would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

***Conclusion***

15. No claim is allowed.

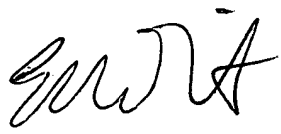
16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The. examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
July 6, 2001



Ethan Whisenant, Ph.D.
Primary Examiner (FSA)